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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,061	07/11/2001	Mohammad Sarwar Nasir	99,576-A	9376

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EXAMINER

DAVIS, DEBORAH A

ART UNIT	PAPER NUMBER
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1641

9

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/903,061

Applicant(s)

NASIR ET AL.

Examiner

Deborah A Davis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

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DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1 and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 6-aminofluorescein, does not reasonably provide enablement for any fluorophore. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Claim 1 is broadly drawn to Deoxynivalenol (DON) conjugated to a fluorophore. The specification, supported by applicant's arguments and declaration only provide support for the 6-aminofluorecein fluorophore (see page 7, line 3 of specification). Applicant has also provided arguments and a declaration stating that only the 6-aminofluorescein fluorophore is able to bind selected antibodies used in the Fluorescence Polarization Assay - asserting that only a certain flouphore, conjugated to DON would produce a detectable change in fluorescence polarization. Applicant is invited to show support in the specification where other fluorophores conjugated to DON are used to detect fluorescence polarization.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-4 and 5-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claims 1 and 5 recite "combining said extract with a tracer" in line 4, is confusing because it is unclear whether the tracer is just the fluorophore or whether the tracer comprise of the extract conjugated to a fluorophore. Please clarify.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 4-6, and 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nasir et al (Fluorescence Polarization, 1999) in view of Pestka et al (Food Technology 1995).

Nasir et al teaches field tests to determine mycotoxins in human, animal and grain diseases and that Fluorescence Polarization is inexpensive and simple to use (pg. 181). Nasir et al teaches a homogenous assay using fluorescence polarization to analyze mycotoxins in grains (See abstract). Mycotoxins that are extracted from grains,

with a suitable solvent and the sample are added into the antibody solution. A mycotoxin antigen of interest is labeled with a fluorescent molecule (tracer) and is added to the antibody solution. Once the reaction takes place, the fluorescent polarization of the tracer is then measured (pg. 182, para. 1).

Nasir et al does not point out if the particular mycotoxin assayed was deoxynivalenol (DON) or its derivative, trichothecenes.

However, Pestka et al teaches immunological assays for the detection of DON and trichothecenes in food. DON and its form trichothecenes, can elicit a variety of toxic symptoms in humans and animals ranging from gastroenteritis to cancer. Besides human health, DON and its derivative, trichothecenes have a major economic impact on live stock productivity as a result of lower quantity and quality of animal products, smaller litters, infertility etc. The Food and Agriculture Organization estimates that 25% of the world's crops are affected by mycotoxins.

It would have been obvious to one of ordinary skill in the art such as Nasir et al to be motivated to detect the levels of deoxynivalenol (DON) and its derivative trichothecenes in food, as taught by Pestka et al, to detect toxic levels of contamination in food. DON and its derivative trichothecenes, and for that matter other mycotoxins are a health hazard to humans and animals and therefore needs to be tested to determine safe and toxic levels in food. Further, one skilled in the art will understand the importance of detecting the above mentioned toxins because they are a public health risk.

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7. Claims 2 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nasir et al in view of Pestka et al, as applied to claims 1, 4-6, and further in view of Michel et al (USP#5,741,654).

The teachings of Nasir et al are set forth above and differ from the instant claim in not particularly pointing out a particular type of fluorescein (6-aminofluorescein) used in the assay.

However, Michel et al discloses a Fluorescence Polarization assay for the quantification of human autoantibodies in which a variety of fluoresceins are used as tracers, such as 5-carboxyfluorescein, thiourefluorescein, and one mentioned in particular is the 6-aminofluorescein moiety which is one of the preferred moieties of choice in the said assay (col. 8, lines 1-22).

It would have been obvious to one of ordinary skill in the art to employ a fluorescein moiety such as any one of the structures named above because they are well known in the art to use in Fluorescence Polarization Immunoassays for quantitation of a sample and either fluorcein used can yield the same results.

8. Claims 3 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nasir et al in view of Pestka et al, as applied to claims 1 and 5, and in further view of McMahon et al (USP#5,166,078).

The teachings of Nasir et al and Pestka et al are set for above and differ from the instant claims in not teaching DON and its derivative Trichothecenes in different known samples to make a standard curve.

However, McMahon et al teaches a method for measuring a hapten that is poorly soluble in an aqueous solution such as mycotoxins (col. 1, lines 29-40). The invention permits fast, safe, and convenient measurements of haptens, which are either insoluble or unstable in aqueous solution by providing standards such as hapten-conjugates that are soluble and stable in aqueous solution. The standards are used to determine the amount of haptens that are present in the assay (col. 1, lines 43-48). To determine the amount of hapten in a sample, the reaction of the hapten and the antibody is compared to the reaction of the hapten-conjugate and the antibody. The conjugates of the invention are used as controls in standard immunoassays (col. 2, lines 29-40). The reactivity of the conjugate are compared to the hapten standards and a standard curve was created relating hapten levels to hapten-conjugate levels (col. 3, lines 9-16).

It would have been obvious to one of ordinary skill in the art to use a plurality of haptens as taught by McMahon et al in standard solutions having different known concentrations and comparing them with hapten-conjugates to create a standard curve to permit fast, safe and convenient measurements of haptens. It would be obvious to combine this teaching into the assay of Nasir et al in further view of Pestka et al being that Nasir et al is assaying for mycotoxins and Pestka et al discloses the importance of testing for these mycotoxins in grain. One skilled in the art of food technology would know that mycotoxins include vomitoxin where said vomitoxins include DON and its derivative Trichothecenes (col. 1, lines 36-38). Further, one skilled in the art would know that certain levels of these mycotoxins found in different amounts of grain are

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toxic to human and animals and a standard curve is needed to compare those levels that would be of concern.

9. Claims 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nasir et al in view of Pestka et al, and Zuk et al (4,281,061).

The teachings of Nasir et al and Pestka et al are set forth above and differ from the instant claims in not teaching the assay in the form of a kit.

Zuk et al. Teach that as a matter of convenience the reagents of an immunoassay can be provided as kits, where the reagents are in predetermined ratios, so as to substantially optimize the sensitivity of the assay in the range of interest " (col. 22, lines 63-66).

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the homogeneous assay for the determination of mycotoxins as taught by Nasir et al in view of Pestka et al in the specific detection of DON and its derivative trichothecenes and format them into a kit, because Zuk et al teaches that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in premeasured amounts, which eliminates the variability that can occur when performing the assay.

Response to Arguments

10. Applicant's arguments filed November 17, 2003 have been fully considered but they are not persuasive.

11. Applicant has presented an amendment supported by a declaration that asserts it would not be obvious to one of ordinary skill in the art to find a suitable tracer and antibody for a Fluorescence Polarization assay and that Examiner has not made a prime facie obviousness case. Applicant presents evidence that experts in the field has difficulties in developing a suitable antibody for a Fluorescence Polarization assay and provides an article "Fluorescence Polarization Immunoassay for Pesticides" (see page 4 of amendment) that asserts some attempts have been made to develop FPIA using antibodies from an ELISA format have failed. This argument is not found persuasive because the article explains that most of the antibodies tested in an ELISA format, were successfully used in a Fluorescence Polarization format. Also, according to the same article, a suitable tracer was found by subtracting the background from corresponding signals before calculating polarization or by measuring the vertical and horizontal signal components of the background fluorescence or scatter (see page 260, column 1, paragraph 2). Further, the reference of Michel et al (USP#5,741,654) discloses a Fluorescence Polarization assay that uses a variety of fluoreceins as tracers wherein the fluorophore 6-aminofluorecein was the preferred moiety (see Michel et al, col. 8, lines 1-22). Therefore it is well known in the art to utilize fluorescent moieties such as fluoresceins in fluorescence polarization techniques, which gives the detection signal

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making it suitable for use in fluorescence polarization assays. Moreover, it is the Examiner's position that the prior art suggests that it is well within the skill of the artisan to find a suitable tracer and antibody utilizing fluorescence polarization assays.

12. Applicant argues that the Pestka reference does not mention the fluorescence polarization technique at all and fail to teach what tracer to use or what antibody to use in a fluorescence polarization assay for DON or other trichothecenes. Applicant argues that Nasir fails to teach what tracer to use or what antibody to use in a fluorescence polarization assay for DON or other trichothecenes and that there is no suggestion to combine the references. This argument is not found persuasive because the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The Nasir et al reference teaches that Fluorescence Polarization (FP) is a powerful technique for analyzing mycotoxins in grains and humans. Nasir et al recited: "work by various groups, including our own, have **demonstrated** that the technique can replace a substantial number of solid phase assays" (see summary). Therefore, Nasir et al not only discloses that fluorescence

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polarization assays are powerful tools for analyzing mycotoxins, but confirms this technique by demonstration. With respect to the Pestka reference, it was not relied upon for its teachings of fluorescence polarization, because it was already taught in the reference of Nasir et al. The Pestka reference was relied upon for its teachings of the toxic effects of mycotoxins, such as DON and trichothecenes, found in food consumed by animals and humans. The Food and Agriculture Organization estimates that 25% of the world's crops are affected by mycotoxins (Pestka, page 120, paragraph 2). Those statistics alone is motivation in itself as to why one of ordinary skill in the art would want to modify the Nasir et al reference, that already teaches a fluorescence polarization assay for mycotoxins, to further include detecting other forms of these mycotoxins such as DON, trichothecenes and others mentioned in the Pestka reference.

Conclusion

13. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah A Davis whose telephone number is (703) 308-4427. The examiner can normally be reached on 8-5 Monday thru Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-

1123.



Deborah A. Davis
CM1, 7D16
December 5, 2003



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12/15/03